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Patterns of healthcare utilisation for respiratory complications of adults with neuromuscular disease: a population study

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TAKE HOME MESSAGE

One third of adults with neuromuscular disease received specialist respiratory care. Emergent healthcare use was substantial, emphasizing an urgent need to improve community and social supports.

TWEET

Emergent healthcare use of neuromuscular disease is substantial; urgent need to improve community and social supports.

ABSTRACT

To quantify health service utilisation including monitoring and treatment of respiratory complications for adults with neuromuscular disease (NMD) identifying practice variation and adherence to guideline recommendations at a population level.

Population-based longitudinal cohort study (2003 to 2015) of adults with NMD using hospital diagnostic and health insurance billing codes within administrative health databases.

We identified 185,586 adults with NMD. Mean age 52 years, 59% female. 41,173 (22%) went to an emergency department (ED) for respiratory complications on average 1.6 times every 3 years; 14,947 (8%) individuals were admitted to hospital 1.4 times every 3 years. Outpatient respiratory specialist visits occurred for 64,084 (35%) with 4 visits every 3 years though substantial variation in visit frequency was found. 157,285 (85%) went to the ED (all cause) almost 4 times every 3 years, 100,052 (54%) were admitted to hospital. Individuals with ALS had more ED visits compared to other types of NMD ($P < 0.0001$).

One third of adults with NMD received respiratory specialist care at a frequency recommended by professional guidelines though substantial variation exists. Emergent healthcare utilisation was substantial, emphasizing the burden of NMD on the healthcare system and urgent need to improve community and social supports, particularly for ALS patients.

KEY WORDS: neuromuscular disease; chronic respiratory failure; health care utilisation; mechanical ventilation

INTRODUCTION

Individuals with neuromuscular disorders (NMD) experience progressive respiratory muscle weakness and are at high risk of respiratory insufficiency [1] due to hypoventilation during sleep [2, 3], recurrent atelectasis, and pneumonia [4] resulting from decreased cough effectiveness [5]. Neuromuscular disorders include a heterogeneous spectrum of diseases that affect muscle and nerve function, many of which are genetic, represent extremely complex pathophysiology, have varying degrees of severity, and require high levels of care [6]. Although some NMD are rare, when considered as a group these disorders are relatively common with an estimated prevalence of about 1 in 3,000 [7].

For most individuals with NMD, increased healthcare requirements related to respiratory problems and the need for assistive respiratory technology indicate progression of disease, and increased morbidity and mortality [8]. Acute respiratory failure due to respiratory infection is a frequent reason for unplanned hospital admission, although there are limited empirical data on patterns of healthcare utilisation in this patient population. Chronic respiratory failure is the most common cause of death [7]. The primary aim of respiratory management is prevention and timely management of respiratory related complications, as well as symptom control [9]. Proactive monitoring of pulmonary function [8], appropriate use of respiratory interventions such as lung volume recruitment [5], manual or mechanical cough augmentation [10], and non-invasive ventilation [11] may either prevent or manage progressive respiratory insufficiency, thus reducing unplanned hospital admissions and improving health related quality of life and longevity.

Several consensus documents inform evidence and expert derived best practices which, when adopted, may reduce clinical practice variation and improve the appropriateness of respiratory assessment and management of individuals with NMD [7, 9, 12-19]. Recommendations for management of respiratory health in this population include: access to respiratory and/or sleep specialists early in the disease course; measurement at baseline and over time of lung function, oximetry, and as indicated CO_2, and outpatient clinic visits to assess respiratory symptom progression every 3, 6 or 12 months dependent on disease progression and initiation of ventilation. Despite these consensus statements, surveys of service providers or care recipients suggest variation in respiratory management practices [20, 21] and respiratory complications remain a primary cause of morbidity and mortality [8].

To address gaps in knowledge related to adherence to guideline recommendations at a population level, we conducted a North American population based cohort study using administrative databases to quantify health service utilisation, with a particular focus on services used for assessing, monitoring, and treating respiratory complications for adults with NMD. We hypothesized that frequency of monitoring and respiratory specialist care would be variable but should increase with initiation of mechanical ventilation. Secondary objectives were to explore: (1) all cause publicly funded health service utilisation; (2) variables associated with emergency department (ED) presentation or hospital admission; and (3) changes in healthcare utilisation before and after initiation of home mechanical ventilation (HMV).

METHODS

We conducted a retrospective longitudinal population-based cohort study from April 1st 2003 to March 31st 2015 using health administrative databases for the province of Ontario, Canada held at the Institute for Clinical Evaluative Sciences (ICES) using unique encoded identifiers to link databases. These databases contain anonymized data for all Ontario residents. Ontario, is the most populous Canadian province with a population of approximately 13 million [22]. Costs of all medically necessary care are covered for all residents by universal public health insurance funded through general taxation. Respiratory equipment such as ventilators, continuous positive airway pressure (CPAP) and bilevel devices is publicly funded through the Assistive Devices Program (ADP).

Data Sources and Population

We linked databases at the level of the individual using unique encoded identifiers to identify: (1) hospitalizations including demographic, diagnostic and procedural data, and in-hospital death in the Discharge Abstract Database; (2) ED presentations in the National Ambulatory Care Reporting System; (3) physician billings including procedures in the Ontario Health Insurance Plan (OHIP) database [23]; (4) approvals of assistive devices including ventilators, suction equipment, and supplies in the ADP database; (5) inpatient rehabilitation using the National Rehabilitation Reporting System; (6) facility based continuing (residential) care services in the Continuing Care Reporting System; (7) home care services using the Home Care Database; and death outside of hospital using the (8) Registered Persons Database. To describe immigration status we used the Immigration, Refugees and Citizenship Canada's Permanent

Resident Database. This database contains individual-level demographic data on all immigrants who became permanent residents between 1985 and 2012. Following well-established methods, both neighbourhood income and urban/rural place of residence were ascertained using postal codes and linking to Statistics Canada census data [24]. To identify respiratory specialist care, we used the ICES Physician Database (IPDB) that contains information about all physicians in Ontario.

We created a cohort of adults aged 18 to 105 years using hospital diagnostic codes (International Classification of Disease (ICD-9, ICD-10) or physician billing codes *a priori* considered specific to NMD within health administration databases from April 1st 2003 to March 31st 2008. Within this 5 year period we sought the first instance of these codes considered the 'most responsible' or secondary contributing diagnoses in the hospitalization database [25] indicating hospital admission with a NMD diagnosis. For individuals with a NMD diagnostic code found using the ambulatory care database, we included only those whose NMD diagnosis was confirmed by looking backwards and forwards in time in the hospitalization database (1998-2014) for a NMD-related hospital admission. For those without hospital admission we reviewed the physician-billing database for NMD-related billing in these years. For individuals identified using the OHIP billing code 349 (NMD diagnosis non-specific), we again looked backwards and forwards in the hospitalization (1998-2014) and ambulatory care (2000-2014) databases to establish NMD diagnosis and sought OHIP billings from a neurologist or for an electromyogram enabling more accurate classification.

We grouped diagnostic codes for NMD (ICD and OHIP) into 12 categories: amyotrophic lateral sclerosis/motor neurone disease (ALS/MND); cerebral palsy [26]; Guillain-Barre [27]; metabolic disorders; multiple sclerosis [28]; muscular dystrophy; myasthenia gravis [29]; neuromuscular disorders (non-specific); neuropathy; post-polio syndrome; spina bifida; and spinal muscular atrophy. For modelling purposes we further grouped these NMD categories as rapidly progressive (ALS/MND), slowly or non-progressive (Guillain-Barre syndrome; myasthenia gravis; neuropathy; post-polio syndrome, spinal muscular atrophy), variably progressive (metabolic disorders; muscular dystrophy; neuromuscular disorders (non-specific)), and other (cerebral palsy; multiple sclerosis; spina bifida) [30]. We used previously validated case definitions for asthma [31], COPD [32], congestive heart failure [33] and ICD-10 codes for cardiomyopathy and arrhythmias. We determined Collapsed Aggregated Diagnosis Groups

(CADG) [34] and calculated the Charlson co-morbidity score considering all hospitalizations within 2 years prior to identification of NMD.

Outcomes

To evaluate healthcare utilisation we followed our 2003-2008 cohort from identification of NMD to March 31st 2015 (minimum of seven years). Our primary outcome was health service utilisation for assessment, monitoring, and management of respiratory complications including respiratory related ED presentations and hospital admissions; consultations with a respiratory specialist (in-hospital and ambulatory/outpatient clinic); pulmonary function testing (PFT); polysomnography (PSG); access to community respiratory therapists; and use of respiratory therapies in the community including oxygen, mechanical ventilation; and airway clearance devices.

Additional healthcare utilisation outcomes: all cause ED visits, hospital and ICU admissions; duration of ED, hospital and ICU stay; outpatient clinic visits and in-patient services by specialists other than respiratory; in-patient rehabilitation; homecare services; and long-term care residence. We examined associations of the *a priori* identified demographic and clinical variables with frequency of ED presentation and hospital admission: NMD category [30]; age; sex; neighbourhood income quintile; rural residence; immigration status; ventilation status; use of other medical technologies, comorbidities i.e., COPD, asthma, CHF, myopathy, arrhythmias; and CADGs [34]. We also compared healthcare utilisation in the one and three years before and after initiation of mechanical ventilation in a subset of the cohort with three years of follow-up data after initiation of mechanical ventilation.

Ethical considerations

We conducted our study according to a pre-specified protocol approved by the Research Ethics Board at Sunnybrook Health Sciences Centre, Toronto, Ontario and according to privacy regulations of ICES.

Statistical analyses

We used descriptive statistics to characterize our cohort. We report counts, overall proportion, and mean (standard deviation (SD)) frequency every three years per individual for rates of healthcare utilisation, as well as mean (SD) and

median (interquartile range (IQR)) duration of healthcare utilisation (i.e., hospital admission). We created generalized linear regression models with negative binomial distribution to examine variables associated with frequency of ED presentation or hospital admissions while controlling for the variables described above and using exposure time as an offset variable. We compared healthcare utilization before and after initiation of HMV using t tests. We conducted analyses in SAS Enterprise Guide 7.1 (SAS Institute Inc., Cary, NC, USA).

RESULTS

In the 5-year cohort creation-period, we identified 185,586 adults with NMD. Of these, we identified 2249 (1.2%) through ED presentation, 10,656 (5.7%) through hospitalization, and 172,681 (93.0%) through physician billing only. At baseline, mean age was 52 years, 59% were female, and 89% lived in an urban location. Asthma (15%) and COPD (12%) were fairly common respiratory comorbidities (Table 1; Supplementary Table 1 for the 12 disease groupings).

Table 1 Cohort characteristics (2003 to 2008)

	Total	Rapidly progressive	Slowly/non-progressive	Variably progressive	Other
Total N	185,586	864	32,054	104,865	47,803
Age (years)					
Mean (SD)	52 (16.4)	71.2 (11.9)	53.51 (16.8)	54.39 (16.1)	45.69 (15.2)
18 - 39	44,044 (23.7)	15 (1.7)	7,023 (21.9)	19,640 (18.7)	17,366 (36.6)
40 - 64	96,903 (52.2)	185 (21.4)	16,330 (50.9)	55,523 (52.9)	24,865 (52.0)
65 +	44,639 (24.1)	664 (76.9)	8,701 (27.1)	29,702 (28.3)	5,572 (11.7)
Sex					
Female	109,919 (59.2)	354 (41.0)	17,796 (55.5)	59,410 (56.7)	32,359 (67.7)
Male	75,667 (40.8)	510 (59.0)	14,258 (44.5)	45,455 (43.4)	15,444 (32.3)
Neighbourhood income quintile[a]					
1 (poorest/lowest)	35,603 (19.2)	194 (22.6)	6,449 (20.2)	19,547 (18.7)	9,413 (19.8)
2	36,884 (19.9)	183 (21.3)	6,794 (21.2)	20,546 (19.7)	9,361 (19.6)
3	36,488 (19.7)	175 (20.4)	6,695 (20.9)	20,324 (19.4)	9,294 (19.5)
4	37,672 (20.3)	153 (17.8)	6,103 (19.1)	21,746 (20.8)	9,670 (20.3)
5 (richest/highest)	38,406 (20.7)	155 (18.0)	5,939 (18.6)	22,394 (21.4)	9,918 (20.8)
Rural residence[b]					
No	164,879 (88.8)	739 (85.5)	28,872 (90.1)	93,349 (89.1)	41,919 (87.8)
Yes	20,604 (11.1)	125 (14.5)	3,172 (9.9)	11,459 (10.9)	5,848 (12.2)
Immigration status[c]					
Citizen	169,504 (91.3)	812 (94.0)	28,072 (87.6)	95,935 (91.5)	44,685 (93.5)
Immigrant[d]	12,917 (7.0)	44 (5.1)	3,230 (10.1)	7,107 (6.8)	2,536 (5.3)
Refugee	3,154 (1.7)	8 (0.9)	752 (2.4)	1,815 (1.7)	579 (1.2)
Comorbidity					
COPD	22,162 (11.9)	264 (30.6)	4,070 (12.7)	14,285 (13.6)	3,543 (7.4)
Asthma	28,720 (15.5)	133 (15.4)	4,769 (14.9)	17,414 (16.6)	6,404 (13.4)
CHF	8,310 (4.5)	134 (15.5)	1,570 (4.9)	5,606 (5.4)	1,000 (2.1)

Charlson Comorbidity Index[e]					
0	28,360 (15.3)	369 (46.4)	5,034 (57.6)	14,822 (53.3)	8,135 (70.5)
1 (1 to 3)	16,871 (9.1)	361 (45.4)	3,050 (34.9)	10,502 (37.8)	2,958 (25.6)
2 (≥4)	3,642 (2.0)	66 (8.3)	650 (7.4)	2,475 (8.9)	451 (3.9)

Note: some percentages may not sum to 100 due to rounding.

Rapidly progressive: Amyotrophic Lateral Sclerosis/motor neurone disease

Slowly/non progressive disease comprises: Guillain-Barre syndrome; myasthenia gravis; neuropathy; post-polio syndrome, spinal muscular atrophy

Variably progressive comprises: metabolic disorders; muscular dystrophy; neuromuscular disorders (non-specific physician billing diagnostic codes)

Other: cerebral palsy; multiple sclerosis; spina bifida.

a Unable to establish for 533 (0.3%) individuals.

b Unable to establish for 103 (0.06%) individuals.

c Unable to establish for 11 (0.0006%)individuals.

d Immigrant is defined as resident within Ontario as holding either Canadian permanent residency status or a work, student, or other form of visa.

e Charlson comorbidity index calculated for those admitted to hospital considering all hospitalizations within 2 years prior to the index event (48,873 patients).

Health service utilisation for respiratory complications

From fiscal years 2003-2014, subsequent to identification of NMD diagnosis, 41,173 (22%) individuals went to the ED for respiratory reasons for a total of 85,066 visits with a median (IQR) length of stay 5.2 (2.5-12.4) hours. 14,947 (8%) individuals were admitted to hospital (24,929 admissions) for respiratory reasons with a median (IQR) length of stay 7 (3-17) days. On average, individuals with NMD went to the ED 1.6 times every 3 years and were admitted to hospital 1.4 times every 3 years for respiratory causes. Outpatient clinic visits to a respiratory specialist occurred for 64,084 (35%) individuals with an average of 4 visits every 3 years, though there was substantial variation in the number of visits per individual and those with ALS/MND or muscular dystrophy had an average of 17 and 7.5 visits per individual every 3 years respectively. In-hospital pulmonologist consultation occurred for 17,489 (9%) with the mean (SD) number of consultations falling from 6.6 (13.7) in 2003-2005 to 4.5 (16.1) in 2012-2014. Pulmonary function testing was conducted in 60,388 (33%) individuals with a mean (SD) number of tests every 3 years for the entire group receiving testing ranging from 1.9 (2.0) in years 2003-2005 to 2.2 (3.4) in years 2012-2014 and similar frequencies for individuals with muscular dystrophy and ALS/MND (Supplementary Table 2). Polysomnography was conducted in 26,070 (14%) individuals with testing frequency every 3 years similar over time (Table 2; See Supplementary Table 2 for all health service utilisation for individuals with muscular dystrophy and ALS/MND). A

publicly funded continuous positive airway pressure (CPAP) device was supplied to 7,737 (4.2%) individuals, long-term oxygen therapy (LTOT) to 4,750 (2.6%), and 1,446 (0.8%) were supplied a publicly funded ventilator (invasive (176) or non-invasive bilevel device (1,270)) for HMV. Over 50% of individuals requiring LTOT had COPD and/or CHF as a comorbidity (Table 3). Only 71 (0.04%) individuals received services from publicly funded respiratory therapy providers in the community, reflective, not of a lack of need but of the lack of public funding in Ontario for community respiratory therapy.

Other health service utilisation

From 2003-2014, subsequent to identification of NMD, 157,285 (85%) individuals went to the ED for 1,202,800 visits (all cause) with a median (IQR) length of stay 19.1 [7.6-47] hours. 100,052 (54%) (301,064 admissions) were admitted to hospital (median (IQR) length of stay 9 (3-28) days). On average, individuals with NMD visited the ED (all-cause) almost 4 times every 3 years and were admitted to hospital (all-cause) twice every 3 years. One or more ICU admissions were required for 29,453 (16%) individuals with a total of 53,200 ICU admissions and a median (IQR) length of stay of 3.6 (1.6-8.4) days. Outpatient clinic visits to physician specialists other than respiratory specialists occurred for 184,950 (99.6%) individuals with average visit frequency every 3 years increasing over time from 23.8 to 30.1; 128,775 (69%) had in-hospital specialist (non-respiratory) consultation (Table 2). The most commonly consulted non-respiratory specialists in the outpatient setting were surgeons (46,760, 25%), family medicine (28,780, 16%), and internal medicine (16,852, 9%); only 18,388 (10%) were seen by a neurologist. Admission to a rehabilitation facility occurred for 13,671 (7.4%) individuals with a median (IQR) length of stay of 28 (14-51) days. Admission to a long-term care facility occurred for 9,042 (4.9%) individuals. Of the cohort, 70,033 (38%) NMD individuals received home care services for a median (IQR) of 32 (9-195) hours overall in the year services were approved. The most common services were from registered nurses (23,831, 13%), case managers (11,914, 6%), and combined personal support/homemaker services (10,178, 5%). In the follow-up period 34,336 (18.5%) died.

Table 2 Health service utilisation after NMD diagnosis

Health service N = 185,586 adults	n (%) patients	Overall visits per individual[a]	Number of visits per three years per individual[b]			
			2003-2005	2006-2008	2009-2011	2012-2014
Respiratory related ED visits	41,173 (22.2)	2.1 (2.6); 1 (1,2)	1.5 (1.2)	1.5 (1.3)	1.6 (1.4)	1.6 (1.6)
Respiratory related hospital admission	14,947 (8.0)	1.7 (1.6); 1 (1,2)	1.4 (1.0)	1.4 (1.0)	1.4 (1.0)	1.4 (1.1)
Pulmonology outpatient clinic	64,084 (34.5)	5.9 (22.4); 2 (1,5)	3.8 (11.8)	3.9 (13.1)	4.1 (11.9)	4.0 (11.6)
Hospital pulmonology consult	17,489 (9.4)	6.6 (28.4); 3 (1,6)	6.6 (13.7)	6.4 (17.9)	5.0 (19.6)	4.5 (16.1)
Pulmonary function tests	60,388 (32.5)	3.2 (5.4; 2 (1,3)	1.9 (2)	2.1 (2.8)	2.2 (3.2)	2.2 (3.4)
Sleep studies	26,070 (14.0)	1.8 (1.2; 1 1,2)	1.5 (0.7)	1.5 (0.8)	1.4 (0.6)	1.4 (0.6)
Outpatient clinic (non-pulmonology)	184,950 (99.6)	94.4 (84.5); 74 (42,121)	23.8 (28.5)	27.8 (28.9)	32.2 (30.2)	30.1 (29.0)
Hospital consult (non-pulmonology)	128,775 (69.4)	20.2 (36.2); 6 (2,22)	12.2 (21.5)	11.9 (22.2)	11 (21.3)	11.1 (21.4)
All cause ED visits	157,285 (84.8)	7.7 (13.4); 4 (2,9)	3.1 (5.2)	3.4 (5.6)	3.7 (6.1)	3.7 (5.5)
All cause hospital admission	100,052 (53.9)	3.0 (3.3); 2 (1,4)	1.8 (1.6)	1.9 (1.6)	1.9 (1.7)	2.0 (1.8)
ICU admission	29,453 (15.9)	1.8 (1.6); 1 (1,2)	1.5 (1.1)	1.5 (1.0)	1.5 (1.1)	1.5 (1.1)

a Values are mean (standard deviation); median (interquartile range) during cohort follow up.

b Calculated for individuals in the cohort requiring these services within each three-year time period.

ED: Emergency department; ICU: intensive care unit.

Table 3 Diagnosis of patients receiving home respiratory support

	CPAP n =7737	LTOT n =4750	HMV n = 1446
Neuromuscular disorders (non-specific)	4713 (60.9)	2500 (52.6)	769 (52.9)
Myasthenia gravis	1255 (16.2)	722 (15.2)	149 (10.2)
Multiple sclerosis	1051 (13.6)	652 (13.7)	124 (8.5)
Muscular dystrophy	334 (4.3)	332 (7)	245 (16.9)
Cerebral palsy	180 (2.3)	170 (3.6)	34 (2.3)
Spina bifida	95 (1.2)	65 (1.4)	36 (2.5)
Neuropathy	46 (0.6)	84 (1.8)	20 (1.4)
Guillain-Barre syndrome	35 (0.5)	44 (0.9)	16 (1.1)
Metabolic disorders	28 (0.4)	99 (2.1)	< 6(NA)
ALS/MND	< 6	80 (1.7)	53 (3.6)
SMA	-	< 6	< 6
Post-polio syndrome	-	-	-
Comorbidities			
COPD	964 (12.5)	1792 (37.7)	283 (19.5)
CHF	248 (3.2)	865 (18.2)	92 (6.3)

CPAP: continuous positive airway pressure; LTOT: long-term oxygen therapy; HMV: home mechanical ventilation; ALS: amyotrophic lateral sclerosis; MND: motor neurone disease; SMA: spinal muscular atrophy; COPD: chronic obstructive pulmonary disease; CHF: chronic heart failure

Variables Associated with ED Presentation or Hospital Admission

Individuals with ALS/MND had more ED visits compared to other types of NMD. Those with variably progressive disease had more hospital admissions (P <0.0001). Individuals with spina bifida, cerebral palsy, or multiple sclerosis had the fewest hospital admissions (P <0.0001). Those in the oldest age category had more ED visits and the most hospital admissions (all P values <.0001). Males, individuals in the poorest income quintile, Canadian citizens (as compared to immigrants or refugees), those living in rural locations, those requiring assistive ventilation or other medical technology had more ED visits and hospital admissions (all P values <.0001). Individuals with comorbidity had more ED visits and hospital admissions, with those with CHF having the most ED visits and those with cardiomyopathy the most hospital admissions (Table 4).

Table 4 Variables associated with the number of ED visits and hospital admissions after NMD diagnosis

	ED visits			Hospital admissions		
Variables	IRR[b]	95% CI	P value	IRR[b]	95% CI	P value
Neuromuscular disease (reference = non or slowly progressive)						

Rapidly progressive	4.36	3.89 - 4.88	<.0001	1.27	0.98 - 1.65	0.0677
Variably progressive	1.12	1.1 - 1.13	<.0001	1.22	1.17 - 1.27	<.0001
Other (spina bifida, cerebral palsy, multiple sclerosis)	1.18	1.16 - 1.2	<.0001	0.84	0.8 - 0.88	<.0001
Age (reference = age 18-39 years)						
40-64 years	0.81	0.8 - 0.83	<.0001	1.06	1.02 - 1.1	0.0044
65 years and older	1.03	1.01 - 1.05	0.0021	2.17	2.08 - 2.27	<.0001
Female	0.89	0.87 - 0.9	<.0001	0.89	0.86 - 0.91	<.0001
Neighbourhood income quintile (reference = 1 poorest/lowest)						
Income quintile 2	0.83	0.82 - 0.85	<.0001	0.86	0.82 - 0.9	<.0001
Income quintile 3	0.76	0.74 - 0.77	<.0001	0.83	0.79 - 0.87	<.0001
Income quintile 4	0.7	0.68 - 0.71	<.0001	0.79	0.76 - 0.83	<.0001
Income quintile 5	0.64	0.63 - 0.65	<.0001	0.72	0.69 - 0.75	<.0001
Rural residence	1.92	1.89 - 1.96	<.0001	1.19	1.13 - 1.24	<.0001
Immigration status (reference = citizen)						
Immigrant	0.63	0.61 - 0.64	<.0001	0.83	0.78 - 0.88	<.0001
Refugee	0.76	0.72 - 0.8	<.0001	0.77	0.68 - 0.86	<.0001
Ventilation status (reference = none)						
Invasive ventilation	2.34	1.82 - 3.01	<.0001	2.83	1.65 - 4.87	0.0002
Non-invasive ventilation	1.69	1.51 - 1.88	<.0001	1.47	1.14 - 1.91	0.003
Use of other medical technology[a]	1.82	1.68 - 1.98	<.0001	3.51	2.98 - 4.12	<.0001
Comorbidities						
COPD	1.41	1.38 - 1.44	<.0001	1.52	1.45 - 1.58	<.0001
CHF	1.71	1.66 - 1.77	<.0001	1.76	1.65 - 1.88	<.0001
Asthma	1.3	1.28 - 1.33	<.0001	1.24	1.19 - 1.29	<.0001
Cardiomyopathy	1.33	1.14 - 1.56	0.0004	2.18	1.59 - 3	<.0001
Arrhythmias	1.45	1.38 - 1.53	<.0001	1.87	1.69 - 2.08	<.0001
Collapsed Aggregated Diagnosis Group (reference = few 1-7)						
Many (8-16)	1.74	1.72 - 1.76	<.0001	1.46	1.42 - 1.51	<.0001
None	0.84	0.79 - 0.89	<.0001	1.1	0.95 - 1.26	0.2092

a individuals requiring any of the following: gastrostomy, ileostomy, colostomy, cystostomy, or pacemaker and functional implants.

b Incidence rate ratio

Health Service Utilisation Before and After Ventilation

For the subset of 552 individuals with home ventilator approval and healthcare utilisation data available in the three years before and three years after approval, we found an increase in the mean number of respiratory specialist outpatient visits per patient from 9 (21.7) to 23 (44.7) visits in three years (P <0.0001). Frequency of PFTs also increased whereas frequency of sleep studies decreased (Table 5). We found no difference in frequency of respiratory-

related or all-cause ED visits, hospital or ICU admissions or length of ED visit or hospital length of stay. ICU length of stay decreased from a mean of 43.7 to 27.3 days (P=0.04).

Table 5 Healthcare utilisation before and after initiation of HMV

N = 552	n (%)[a]	Overall prior[b]	Overall after[c]	P value	n (%)[d]	1 year prior	1 year after	P value
Respiratory related ED visits	196 (36)	1.7 (1.9)	1.7 (1.8)	0.95	136 (27)	1.4 (1.3)	1.4 (1.0)	0.72
Length of ED visit , hrs,	-	17.0 (31.8)	16.9 (23.6)	0.97	-	18.9 (32.6)	14.5 (21.4)	0.32
Respiratory related hospital admission	162 (29)	1.7 (1.4)	1.6 (1.4)	0.62	132 (27)	1.5 (1.2)	1.4 (1.0)	0.70
Length of hospital stay, days	-	30.8 (42.9)	22.9 (36.9)	0.17	-	30.5 (43.4)	24.2 (43.0)	0.38
Respirology outpatient clinic	443 (80)	8.9 (21.7)	22.7 (44.7)	<0.0001	443 (89)	7.4 (20.6)	10.5 (20.1)	0.02
Hospital respirology consult	47 (9)	7.9 (12.9)	12.3 (28.2)	0.07	47 (9)	7.3 (11.0)	8.7 (13.7)	0.39
Pulmonary function tests	465 (84)	3.1 (3.0)	4.1 (7)	0.02	448 (90)	2.3 (1.7)	2.8 (5.1)	0.10
Sleep studies	251 (51)	1.6 (0.9)	1.3 (0.6)	<0.0001	229 (46)	1.4 (0.6)	1.1 (0.3)	<0.0001
All cause ED visits	464 (45)	3.9 (4.5)	3.7 (4.9)	0.53	407 (82)	2.4 (2.5)	2.4 (2.5)	0.81
Length of ED visit, hrs	-	25.4 (35.4)	30.9 (44.3)	0.06	-	19.8 (27.6)	19.7 (25.6)	0.93
All cause hospital admission	406 (74)	2.2 (1.8)	2.2 (2.0)	0.77	347 (70)	1.7 (1.2)	1.7 (1.2)	0.52
Length of hospital stay, days	-	39.0 (81.2)	35.4 (75.7)	0.57	-	37.7 (80.7)	33.0 (81.1)	0.59
ICU admission	224 (41)	2 (1.72)	2 (1.6)	0.80	175 (35)	1.9 (1.3)	1.6 (1.2)	0.07
Length of ICU admission, days	-	43.6 (73.5)	27.3 (55.8)	0.04	-	47.0 (77.7)	28.9 (63.4)	0.07
Ventilated ICU admission	50 (9)	2.4 (1.9)	2.3 (1.6)	0.89	44 (9)	2.3 (1.71)	1.8 (0.9)	0.11
Length of ventilated admission	-	75.0 (88.8)	34.8 (48.0)	0.02	-	72.1 (88.1)	31.9 (52.5)	0.04

All values are means (standard deviation) unless otherwise indicated. ALS/MND = 23; Cerebral palsy = 20; Guillain-Barre syndrome < 6; metabolic disorders = 7; multiple sclerosis = 15; muscular dystrophy = 52; myasthenia gravis = 59; neuromuscular disorders (non-specific) = 355; neuropathy = 7; post-polio syndrome < 6; spina bifida = 6; spinal muscular atrophy < 6.

a n (%) of individuals that utilized these healthcare services in both the 3 years preceding and the 3 years following approval for publically funded HMV.

b calculated for the 3 years prior to initiation of HMV.

c calculated for 3 years after initiation of HMV.

d n (%) of individuals that utilized these healthcare services one year before and one year after initiation of HMV

DISCUSSION

In this retrospective longitudinal population based study of adults with NMD, we found the burden of acute healthcare utilisation associated with respiratory complications was moderate with 22% visiting ED, on average 1.6 times every 3 years and 8% requiring hospital admission, on average 1.4 times every 3 years. Interestingly, of those admitted to hospital for respiratory complications, only 9% had an in-patient respiratory specialist consultation. One third of our cohort saw respiratory specialists in an outpatient setting on average every nine months and underwent PFT monitoring on average every 18 months. In comparison, based on health administration database documentation of physician specialty, a neurologist saw only 10% of our cohort of adults with NMD. Approximately 6% of the cohort experienced substantial respiratory comorbidity requiring LTOT, CPAP, or HMV. Approval for HMV was accompanied by an increase in respiratory specialist outpatient visits and assessment of PFTs in the subsequent three years but did not affect the frequency of ED visits or hospitalization.

In this real-world study, for those individuals who received specialist respiratory care, on average frequency of access to respiratory specialists, PFT and PSG monitoring reflects current guideline recommendations, although we found considerable variability particularly in terms of frequency of clinic visits. The American Thoracic Society [12, 35] and Centre for Disease Control and Prevention (CDC) guidelines [9, 13] recommend monitoring and treatment of respiratory complications should be performed by respiratory specialists with clinic visits every 3 to 12 months depending on disease progress. Similarly, evaluation of PFTs are recommended at baseline and with increasing in frequency for those with progressive disease. Reasons for wide variation in visit frequency may be attributed to the variable disease progression in NMD, but may also reflect variability in access to specialist respiratory care. Comparison with international practice is challenging as data are limited and are not reported at a population level. In a US database describing respiratory care over 11 years for 208 males with Duchenne muscular dystrophy, a group with progressive disease and generally adherent with therapy with a good response to respiratory interventions, fewer than 32% were evaluated by a respiratory specialist in the year 2010-2011 and no more than 50% had PFTs measured twice yearly [8]. In a 2011-12 cross sectional European survey, again of Duchenne muscular dystrophy reporting on 1062 individuals, pulmonary function was not assessed regularly in 71% of non-ambulatory patients [36]. As

described below, we were unable to isolate Duchenne muscular dystrophy within health administrative databases to enable comparison.

Our data demonstrate the considerable burden of NMD on the public healthcare system. *All cause* public health service utilisation for individuals with NMD was substantial with 85% visiting the ED on average more than once a year, equivalent to over 1.2 million visits in 12 years, over 50% requiring hospitalization on average twice every three years, and 16% requiring ICU admission, twice on average during cohort follow up. After adjusting for multiple factors, patients with ALS were the highest users of the ED among our cohort. Reasons for high use of emergent care likely include lack of access to specialty care, lack of care integration, lack of respite, and inexperience of general practitioners with this disease [37, 38]. From our data, we can conclude that strategies are needed urgently to improve community and social supports for all patients with NMD that minimize emergent healthcare utilisation, but particularly those with ALS.

Provision of publicly funded respiratory devices and community respiratory therapy was low considering the level of respiratory morbidity of the cohort. In Ontario, although all approvals for publicly funded non-invasive and invasive ventilators are captured in the Assistive Devices Program database, other respiratory equipment including CPAP and bilevel devices may be obtained from non-publicly funded sources or purchased by individuals [39], and therefore our data may underestimate the use of respiratory support for NMD. Furthermore, availability of respiratory therapists in the community is extremely limited in Ontario [40]. Interestingly, despite a considerable increase in the frequency of PFT monitoring and respiratory specialist review after HMV commencement, there was no difference in the need for emergent care or hospital admission. Reasons for this might reflect ongoing disease progression or may relate to the limited availability of community healthcare workers for ventilator assisted individuals [41].

A major strength of our study that provides unique data on the respiratory management of NMD is the use of real world data from health administrative databases to capture health utilisation on a population based level. Our study has limitations. We cannot rule out misclassification, under, or over ascertainment, particularly using physician billing codes to identify NMD. The non-specific neuromuscular category comprised individuals identified with the OHIP

billing code 349 that likely included individuals with ALS/MND and muscular dystrophy for whom we were unable to further delineate diagnosis through an ICD code. Limitations of health administrative database coding prevented more disease specific description of healthcare utilisation i.e., Duchenne muscular dystrophy, the most common muscular dystrophy, as well as an accurate estimation of disease progression on an individual patient level or within disease categories. We were unable to account for other potential confounders of ED presentation or hospital admission such as patient mobility status and the primary language spoken as these data are not available in health administrative databases. Additionally, health administrative databases do not enable us to assess if all individuals with NMD that should have received specialist respiratory care, did receive this care. Lastly, we were unable to assess use of airway clearance strategies as mechanical insufflation-exsufflation devices were publicly funded only from 2014 onwards, prior to this date devices were covered by third party insurers or personal expense.

CONCLUSION

In this heterogeneous population of adults with NMD, we found approximately one fifth required emergent care for respiratory complications and one third received ongoing respiratory specialist care. For those receiving this care, frequency of monitoring adhered to guideline recommendations however substantial variation was noted which likely reflects variable disease progression but also variable access to specialist care. Emergent healthcare utilisation was substantial, emphasizing the burden of NMD on the healthcare system and the urgent need to improve community and social supports, particularly for ALS patients.

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AUTHOR CONTRIBUTIONS

Author Contributions: LR, DM, RA, SK conceived of the study; all authors were involved in design of the study; LR and AG have been involved in cohort creation; all authors have contributed to analysis and interpretation of the data and writing the article before submission.

CONFLICT of INTEREST

The authors have no conflicts of interest to declare.

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REFERENCES

1. Hill N. Ventilator management for neuromuscular disease. *Semin Respir Crit Care Med* 2002: 23: 293-305.
2. Tzeng A, Bach J. Prevention of pulmonary morbidity for patients with neuromuscular disease. *Chest* 2000: 118: 1390–1396.
3. Panitch H. The pathophysiology of respiratory impairment in pediatric neuromuscular diseases. *Pediatrics* 2009: 123: S215–S218.
4. Gomez-Merino E, Bach J. Duchenne muscular dystrophy: prolongation of life by noninvasive ventilation and mechanically assisted coughing. *Am J Phys Med Rehabil* 2002: 81: 411–415.
5. McKim D, Katz S, Barrowman N, Ni A, LeBlanc C. Lung volume recruitment slows pulmonary function decline in Duchenne muscular dystrophy. *Arch Phys Med Rehabil* 2012: 93: 1117-1122.
6. Howard R. Respiratory failure because of neuromuscular disease. *Curr Opin Neurol* 2016: 29: 592-601.
7. Hull J, Aniapravan R, Chan E, Chatwin M, Forton J, Gallagher J, Gibson N, Gordon J, Hughes I, McCulloch R, Russell R, Simonds A. British Thoracic Society guideline for respiratory management of children with neuromuscular weakness. *Thorax* 2012: 67: 1-40.
8. Andrews J, Soim A, Pandya S, Westfield C, Ciafaloni E, Fox D, Birnkrant D, Cunniff C, Sheehan D, Muscular Dystrophy Surveillance T, and Research Network (MD STARnet). Respiratory care received by individuals with Duchenne Muscular Dystrophy from 2000 to 2011. *Respir Care* 2016: 61: 1349-1359.
9. Bushby K, Finkel R, Birnkrant D, Case L, Clemens P, Cripe L, Kaul A, Kinnett K, McDonald C, Pandya S, Poysky J, Shapiro F, Tomezsko J, Constantin C, DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. *Lancet Neurol* 2010: 9: 177-189.
10. Bach JR. Respiratory muscle aids to avert respiratory failure and tracheostomy: A new patient management paradigm. Can J Respir Ther 2010: 46: 24-32.
11. Bach JR, Martinez D. Duchenne muscular dystrophy: Continuous noninvasive ventilatory support prolongs survival. *Respir Care* 2011: 56: 744-750.
12. Finder J, Birnkrant D, Carl J, Farber H, Gozal D, Iannaccone S, Kovesi T, Kravitz R, Panitch H, Schramm C, Schroth M, Sharma G, Sievers L, Silvestri J, Sterni L, American Thoracic Society. Respiratory care of the patient with Duchenne muscular dystrophy: ATS consensus statement. *Am J Respir Crit Care Med* 2004: 170: 456-465.

13. Birnkrant D, Bushby K, Amin R, Bach J, Benditt J, Eagle M, Finder J, Kalra M, Kissel J, Koumbourlis A, Kravitz R. The respiratory management of patients with Duchenne muscular dystrophy: a DMD Care Considerations Working Group specialty article. Pediatr Pulmonol 2010: 45: 739-748.
14. Wang C, Bonnemann C, Rutkowski A, Sejersen T, Bellini J, Battista V, Florence J, Schara U, Schuler P, Wahbi K, Aloysius A, Bash R, Béroud C, Bertini E, Bushby K, Cohn R, Connolly A, Deconinck N, Desguerre I, Eagle M, Estournet-Mathiaud B, Ferreiro A, Fujak A, Goemans N, Iannaccone S, Jouinot P, Main M, Melacini P, Mueller-Felber W, Muntoni F, Nelson L, Rahbek J, Quijano-Roy S, Sewry C, Storhaug K, Simonds A, Tseng B, Vajsar J, Vianello A, R Z, International Standard of Care Committee for Congenital Muscular Dystrophy. Consensus statement on standard of care for congenital muscular dystrophies. *J Child Neurol* 2010: 25: 1559-1581.
15. ACI Respiratory Network. Domiciliary non-invasive ventilation in adult patients: a consensus statement. Chatswood, NSW: Agency for Clinical Innovation; 2012.
16. Miller R, Jackson C, Kasarskis E, England J, Forshew D, Johnston W, Kalra S, Katz J, Mitsumoto H, Rosenfeld J, Shoesmith C, Strong M, Woolley S, Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2009: 73: 1218-1226.
17. McKim D, Road J, Avendano M, Abdool S, Cote F, Duguid N, Fraser J, Maltais F, Morrison D, O'Connell C, Petrof B, Rimmer K, Skomro R, Canadian Thoracic Society Home Mechanical Ventilation Committee. Home mechanical ventilation: a Canadian Thoracic Society clinical practice guideline. *Can Respir J* 2011: 18: 197-215.
18. Windisch W, Geiseler J, Simon K, Walterspacher S, Dreher M, Guideline Commission. German national guideline for treating chronic respiratory failure with invasive and non-invasive ventilation: revised edition 2017 - part 1. *Respiration* 2018: 1-32.
19. Windisch W, Geiseler J, Simon K, Walterspacher S, Dreher M, Guideline Commissio. German national guideline for treating chronic respiratory failure with invasive and non-invasive ventilation: revised edition 2017 - part 2. *Respiration* 2018: 1-32.
20. Katz S, McKim D, Hoey L, Barrowman N, Kherani T, Kovesi T, MacLusky I, Mah J. Respiratory management strategies for Duchenne muscular dystrophy: practice variation amongst Canadian sub-specialists. *Pediatr Pulmonol* 2013: 48: 59-66.

21. Hannan L, Sahi H, Road J, McDonald C, Berlowitz D, Howard M. Care practices and health-related quality of life for individuals receiving assisted ventilation. A Cross-National Study. *Ann Am Thorac Soc* 2016: 13: 894-903.
22. Statistics Canada. 2011 Census profile. 2013 [Accessed 28th Nov 2017]; Available from: http://www12.statcan.gc.ca/census-recensement/index-eng.cfm
23. Herring A, Ginde A, Fahimi J, Alter H, Maselli J, Espinola J, Sullivan A, Camargo CJ. Increasing critical care admissions from U.S. emergency departments, 2001-2009. *Crit Care Med* 2013: 41: 1197-1204.
24. Stephenson A, Hux J, Tullis E, Austin P, Corey M, Ray J. Socioeconomic status and risk of hospitalization among individuals with cystic fibrosis in Ontario, *Canada. Pediatr Pulmonol* 2011: 46: 376–384.
25. Juurlink D, Preyra C, Croxford R, Chong A, Austin P, Tu J, Laupacis A. Canadian Institute for Health Information Discharge Abstract Database: A validation study. Toronto: Institute for Clinical Evaluative Sciences; 2006.
26. Ray J, Redelmeier D, Urquia M, Guttmann A, McDonald S, Vermeulen M. Risk of cerebral palsy among the offspring of immigrants. *PLoS One* 2014: 9: e102275.
27. Breiner A, Widdifield J, Katzberg H, Barnett C, Bril V, K T. Epidemiology of myasthenia gravis in Ontario, Canada. *Neuromuscul Disord* 2016: 26: 41-46.
28. Widdifield J, Ivers N, Young J, Green D, Jaakkimainen L, Butt D, O'Connor P, Hollands S, Tu K. Development and validation of an administrative data algorithm to estimate the disease burden and epidemiology of multiple sclerosis in Ontario, Canada. *Mult Scler* 2015: 21: 1045-1054.
29. Kwong J, Vasa P, Campitelli M, Hawken S, Wilson K, Rosella L, Stukel T, Crowcroft N, McGeer A, Zinman L, Deeks S. Risk of Guillain-Barré syndrome after seasonal influenza vaccination and influenza health-care encounters: a self-controlled study. *Lancet Infect Dis* 2013: 13: 769-776.
30. Shneerson J, Simonds A. Noninvasive ventilation for chest wall and neuromuscular disorders. *Eur Respir J* 2002: 20: 480-487.
31. Gershon A, Wang C, Guan J, Vasilevska-Ristovska J, Cicutto L, To T. Identifying patients with physician-diagnosed asthma in health administrative databases. *Can Respir J* 2009: 16: 183-188.
32. Gershon A, Wang C, Guan J, Vasilevska-Ristovska J, Cicutto L, To T. Identifying individuals with physcian diagnosed COPD in health administrative databases. *COPD* 2009: 6: 388-394.
33. Schultz S, Rothwell D, Chen Z, Tu K. Identifying cases of congestive heart failure from administrative data: a validation study using primary care patient records. *Chronic Dis Inj Can* 2013: 33: 160-166.

34. Austin P, van Walraven C, Wodchis W, Newman A, Anderson G. Using the Johns Hopkins Aggregated Diagnosis Groups (ADGs) to predict mortality in a general adult population cohort in Ontario, Canada. *Med Care* 2011: 49: 932-939.
35. Finder J. A 2009 perspective on the 2004 American Thoracic Society statement, "respiratory care of the patient with Duchenne muscular dystrophy". *Pediatrics* 2009: 123: S239-241.
36. Vry J, Gramsch K, Rodger S, Thompson R, Steffensen B, Rahbek J, Doerken S, Tassoni A, Beytía M, Guergueltcheva V, Chamova T, Tournev I, Kostera-Pruszczyk A, Kaminska A, Lusakowska A, Mrazova L, Pavlovska L, Strenkova J, Vondráček P, Garami M, Karcagi V, Herczegfalvi Á, Bushby K, Lochmüller H, Kirschner J. European cross-sectional survey of current care practices for Duchenne Muscular Dystrophy reveals regional and age-dependent differences. *J Neuromuscul Dis* 2016: 3: 517–527.
37. Hobson E, Baird W, Partridge R, Cooper C, Mawson S, Quinn A, Shaw P, Walsh T, Wolstenholme D, Mcdermott C. The TiM system: developing a novel telehealth service to improve access to specialist care in motor neurone disease using user-centered design. *Amyotroph Lateral Scler Frontotemporal Degener* 2018: 1-11.
38. Peters M, Fitzpatrick R, Doll H, Playford E, Jenkinson C. Patients' experiences of health and social care in long-term neurological conditions in England: a cross-sectional survey. *J Health Serv Res Policy* 2013: 18: 28-33.
39. Rose L, McKim D, Katz S, Leasa D, Nonoyama M, Pedersen C, Goldstein R, Road J, Group C. Home mechanical ventilation in Canada: a national survey. *Respir Care* 2015: 60: 695-704.
40. Leasa D, Elson S. Building a comprehensive system of services to support adults living with long-term mechanical ventilation. *Can Resp J* 2016: 2016: ID 3185389.
41. Dale C, King J, Nonoyama M, Carbone S, McKim D, Road J, Rose L, CANuVENT group. Transitions to home mechanical ventilation: the experiences of Canadian ventilator-assisted adults and their family caregivers. *Ann Am Thorac Soc* 2017: doi: 10.1513/AnnalsATS.201708-201663OC.